Attorney Docket No.: JB06017US01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appl. No.	:	10/822,254
Applicant	:	Taremi et al.
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TC/AU	:	1656
Examiner	:	David J. Steadman
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Schering-Plough Corporation
Kenilworth, New Jersey 07033-0530

Mail Stop: Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF UNDER 37 C.F.R. § 41.37

Sir:

This appeal is taken from the decision of the Primary Examiner, mailed on April 15, 2008, in which claims of the subject application were finally rejected and from a Pre-Appeal Board decision in connection therewith (mailed August 22, 2008). Further to the Notice of Appeal filed on July 15, 2008, this Appeal Brief is being provided along with a fee transmittal sheet, in duplicate, for charging the appeal brief fee and the fee for a three month extension of time. The USPTO is authorized to charge the necessary fees to account no. 19-0365.

TABLE OF CONTENTS

REAL PARTY IN INTEREST

The real party in interest in this appeal is Schering Corporation, 2000 Galloping Hill Road, Kenilworth, New Jersey 07033, assignee of the above identified application by virtue of an assignment executed by the inventors.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any other appeals, or interferences, for the above identified application which relate to, directly affect, will be directly affected by or have a bearing on the Board's decision in this Appeal.

STATUS OF CLAIMS

The table set forth below indicates the status of each claim in the instant case.

Claim	Status
1	Cancelled
2	Rejected, on appeal
3	Cancelled
4	Cancelled
5	Cancelled
6	Cancelled
7	Cancelled
8	Cancelled
9	Cancelled
10	Cancelled
11	Cancelled
12	Cancelled
13	Cancelled
14	Allowed
15	Cancelled
16	Cancelled
17	Cancelled
18	Cancelled
19	Cancelled
20	Cancelled
21	Cancelled
22	Cancelled

23	Cancelled
24	Cancelled
25	Cancelled
26	Cancelled
27	Cancelled
28	Allowed
29	Cancelled
30	Allowed
31	Cancelled
32	Cancelled
33	Cancelled
34	Allowed
35	Allowed
36	Rejected, on appeal
37	Rejected, on appeal
38	Rejected, on appeal
39	Rejected, on appeal

STATUS OF AMENDMENTS

A final rejection was made in the office action mailed April 15, 2008. No amendment was entered in response to this action.

An amendment under 37 C.F.R. § 1.116 was filed with the corrected version of this Appeal Brief submitted in response to the Notice of Non-compliant Brief that was mailed on January 29, 2009. This amendment has not yet been entered.

SUMMARY OF CLAIMED SUBJECT MATTER

The following is a summary of the invention covered by the independent claims under appeal. The required references to specification pages and line numbers are set forth in the text of the Summary in parentheses.

The claimed subject matter under appeal includes:

Independent Claim 2: A purified polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 6 (Sequence Listing at SEQ ID NO: 6; page 4, lines 11-25; page 23, lines 5-8), SEQ ID NO: 8 (Sequence Listing at SEQ ID NO: 8; page

4, lines 11-25; page 23, lines 9-12), SEQ ID NO: 10 (Sequence Listing at SEQ ID NO: 10; page 4, lines 11-25; page 23, lines 13-16) and SEQ ID NO: 12 (Sequence Listing at SEQ ID NO: 12; page 4, lines 11-25; page 23, lines 17-20).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether the claims covering the HDM2 polypeptides (2 and 36-39) are sufficiently described and, thus, in compliance with the Written Description requirement.

Whether the claims covering the HDM2 polypeptides (2 and 36-39) are supported by an enabling disclosure and, thus, in compliance with the Enablement requirement.

GROUPING OF CLAIMS

The grounds for rejection for alleged lack of Written Description and Enablement appear to apply equally to all rejected and appealed claims. The rejected and appealed claims stand and fall together.

ARGUMENT

Claim rejections under 35 U.S.C. § 112(¶1)-Written Description

Claims 2, 15 and 36-39 stand rejected for an alleged lack of written description. The claims are directed, very generally, to "purified polypeptide[s]". The Examiner contended that these claims encompassed a very large genus insofar as they cover all possible crystalline polypeptides; whereas, the specification only describes a few crystalline species of the claimed genus. Thus, the examiner argued, the claimed genus is not sufficiently described. The examiner took the position that only claims directed to non-crystalline polypeptides would be adequately

described (see October 26, 2007 Office Action at page 5, last paragraph).

The applicants do not disagree with the examiner's interpretation as to the scope of the instant claims. *Any* purified polypeptide, crystalline or non-crystalline, comprising the elements specified in the claims, is encompassed.

The applicants believe, however, that the examiner is incorrect with respect to the Written Description standard. This position is based on both the case law and various pronouncements of patent examination policy by the USPTO. Indeed, the case law has held, for many years, that disclosure of a polypeptide's structure in the form of an amino acid sequence is sufficient description for the type of claims sought. The applicants are unaware of any court opinion or USPTO guideline or commentary interpreting the Written Description requirement otherwise. This amounts to a truly new and, heretofore, unheard-of requirement for patentability which the examiner is arbitrarily imposing on the applicants.

The case law discussed below concerned claims covering polynucleotides and polypeptides wherein the amino acid or nucleotide sequence was adequate description in spite of the fact that the disputed claims encompassed crystals (claim construction is discussed in detail below). Though the courts do not appear to have addressed this issue head-on, the case law points to an understanding of the Written Description requirement which dictates that the amino acid sequence of a claimed polypeptide is sufficient disclosure of its structure to establish possession of the polypeptide *in all physical forms.*

At the outset, narrowing the claims will not necessarily narrow the amount of written description necessary for compliance with the rule. The examiner's suggestion to narrow the claims to

non-crystalline polypeptides suggests a misunderstanding of this point. Indeed, the pending claims may require less written support than if they were limited to non-crystalline polypeptides. The examiner's apparent belief that the quantity of necessary written support always correlates directly with the scope of the claim is incorrect. The Courts have ruled that claims with additional limitations (*i.e.*, narrower claims) may require additional written support for those limitations; whereas, claims without such limitations (*i.e.*, broader claims) may be compliant with the Written Description requirement even in the absence of such support. For example, in *In re Smith*, the CCPA pointed out that a given description may be sufficient to support a broad claim, but not a narrow claim. 59 C.C.P.A. 1025 (C.C.P.A. 1972). The applicant, in *Smith*, argued that if a broad genus covering an emulsive coating were described and, thus, entitled to priority under 35 U.S.C. § 120, then a narrower subgenus must also be entitled to priority. *Id.* at 1032. The Court disagreed stating "We see nothing inherently wrong with a particular principle of patentability which under certain circumstances operates to defeat the patentability of a narrow, but not a broader, claim, and, ordinarily, the mere fact that under such a principle a broader claim would pass muster is not a basis for adjusting the principle to render the narrower claim patentable." *Id.* at 1034. Thus, a corollary to this holding is that additional description of crystals is not required to support claims covering any purified polypeptide merely because they may encompass such crystals. Indeed, in view of *Smith*, the instant claims may be supported *even more* firmly by the specification than the suggested non-crystalline claims. This principle is in accord with later case law relating to written description.

Fiers, *Lilly* and *Invitrogen* (discussed below) stand for the position that disclosure of a nucleotide or amino acid sequence in a case claiming, generally, "An isolated polypeptide" or "An isolated polynucleotide" is sufficient description. None of the cases recite the additional requirement of, for example, description of crystalline forms of the claimed molecules, or, in the absence of such data, exclusion of such crystals from the claims.

In *Fiers v. Revel*, the Federal Circuit held that the nucleotide sequence of a claimed DNA molecule (not limited to non-crystalline molecules) constitutes adequate written description. *Fiers v. Revel*, 984 F.2d 1164, 1172 (Fed. Cir. 1993). In *Fiers*, an issue was whether appellee-Sugano was entitled to his priority date for DNA encoding interferon. *Id.* at 1167-1169. The *Fiers* Court held that Sugano was entitled to his filing date since he had satisfied the Written Description requirement with regard to the claimed DNA. *Id.* at 1172. Specifically, the Court found that, as of this date, Sugano had provided a complete sequence for the claimed molecule. The *Fiers* Court stated as follows:

> We also conclude that Sugano's application satisfies the written description requirement since it sets forth the complete and correct nucleotide sequence of a DNA coding for B-IF and thus "convey[s] with reasonable clarity to those skilled in the art that, as of the filing date sought, [Sugano] was in possession of the [DNA coding for B-IF]. (emphasis added)
> *Id.*

Fiers relates to the description of DNA and not protein; however, its holding can clearly be applied to the instant case. Both DNA and protein are polymeric biomolecules, composed of a

limited number of types of subunits, which can exist in crystalline or non-crystalline forms. The Federal Circuit has seen fit to extend Written Description holdings relating to genetic material to cases concerning non-genetic inventions. In *Univ. of Rochester v. G.D. Searle & Co.*, the invention at issue concerned whether a method for selectively inhibiting COX-2 was adequately described. 358 F.3d 916, 918 (Fed. Cir. 2004). The appellant sought to distinguish the holdings of *Lilly*, *Fiers* and *Enzo* from the case since these holdings dealt with inventions of genetic material. *Id.* at 925. The court rejected this argument stating:

> We agree with Rochester that *Fiers*, *Lilly*, and *Enzo* differ from this case in that they all related to genetic material whereas this case does not, but we find that distinction to be unhelpful to Rochester's position. It is irrelevant; the statute applies to all types of inventions. We see no reason for the rule to be any different when non-genetic materials are at issue;
> *Id.*

Analogously, it would be appropriate to extend these cases to the present invention notwithstanding the fact that it relates to polypeptides. Such action would clearly be appropriate in view of the court's opinion on this issue.

Later, *Fiers* was cited in the holding of the case of *Regents of University of California v. Eli Lilly & Co.* 119 F.3d 1559, 1566-1567 (Fed. Cir. 1997). In *Lilly*, the Federal Circuit addressed whether claims covering a plasmid containing cDNA encoding insulin, were sufficiently described. *Id.* at 1566. The Court found the claims invalid because the cDNA was not sufficiently described. *Id.* at 1569. In making this finding, the Court exemplified what is necessary for cDNA to be

sufficiently described. The Court, referring to *Fiers*, stated that compliance with the requirement "requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA." *Id.* Thus, again, the courts demonstrated that claims covering polymeric biomolecules, such as protein and DNA, are sufficiently described by their amino acid or nucleotide sequences, respectively. Though the claims at issue, in *Lilly*, would have covered crystalline and non-crystalline DNA alike, the court made no mention of any requirement to limit the claims to non-crystalline DNA.

A further relevant case from the Federal Circuit is *Invitrogen Corp. v. Clontech Labs., Inc.* In this case, the Court examined whether a patent directed to a polypeptide with DNA polymerase activity was compliant with the Written Description requirement. 429 F.3d 1052, 1072 (Fed. Cir. 2005). A claim, pointed out by the Court, read as follows:

> 1. An isolated polypeptide having DNA polymerase activity and substantially reduced RNase H activity, wherein said polypeptide is encoded by a modified reverse transcriptase nucleotide sequence that encodes a modified amino acid sequence resulting in said polypeptide having substantially reduced RNase H activity, and wherein said nucleotide sequence is derived from an organism selected from the group consisting of a retrovirus, yeast, Neurospora, Drosophila, primates and rodents. *Id.*

The specification provided an amino acid sequence wherein related sequences were known in the art. *Id.* at 1073. The Court found the claims to be sufficiently described, in part, because "the shared written description for the patents-in-issue recites both the DNA and amino acid sequences of a representative

embodiment of the claimed RT enzyme." *Id.* Here, the Court found the claimed polypeptides to be sufficiently described on the basis of disclosure of amino acid sequence data.

Furthermore, as mentioned above, the USPTO Written Description Guidelines and the Office's expressions of official policy in reports of the Trilateral Project further substantiate the applicants' point. In these sources, claims worded analogously to the instant claims were found described on the basis of the amino acid sequence. None of the claims were limited to non-crystalline polypeptides.

Example 13 of the Written Description Guidelines considered a hypothetical claim:

> 1. An isolated protein having SEQ ID NO: 3.

; wherein the hypothetical specification disclosed the SEQ ID NO: 3 amino acid sequence. This claim was adequately described in spite of the fact that no description of crystalline molecules was mentioned in the hypothetical specification and the claims did not exclude crystalline proteins.

The Trilateral Project "Report on Comparative Study on Biotechnology Patent Practices Carried Out Under Trilateral Project B3b" provides further support. In example 1 of "Annex 1: Comments of the USPTO", the USPTO discussed an application with the hypothetical claim:

> 1. An isolated and purified receptor the sequence of which consists of SEQ ID NO: 1

SEQ ID NO: 1 was an amino acid sequence. This claim was adequately described. Again, the claims did not exclude crystalline receptors and there was no mention of a description of all crystals in the specification.

In case 5 of the USPTO comments in the Trilateral Project WM4, "Comparative study on protein 3-dimensional (3-D) structure related claims", the hypothetical applicants sought the following two claims:

> Claim 1: An isolated and purified molecule comprising a binding pocket of protein P defined by the structural coordinates of amino acid residues 223, 224, 227, 295, 343, 366, 370, 378 and 384 according to Figure 1.
>
> Claim 2: An isolated and purified polypeptide consisting of a portion of protein P starting at one of amino acids 214 to 218 and ending at one of amino acids 394 to 401 of protein P as set forth in SEQ ID NO: 1.

The hypothetical specification discussed the 3-dimensional structure of the polypeptide, stating:

> The description teaches that all possible peptides that begin with any amino acid from position 214 to 218 and end with any amino acid from position 394 to 401 of SEQ ID NO: 1 are protein domains that fold into an active binding pocket of protein P. This ability was confirmed by X-ray diffraction data.

Here, the specification specifically discussed a crystal of the claimed protein. A counter-argument offered by the examiner (discussed in greater detail below) was that the Comments presented were inapplicable because these sources did not relate, explicitly, to crystalline molecules. Even if the examiner is correct on this point (which we do not concede), these claims would undoubtedly encompass crystals. Nevertheless, the claims, as written, were found to be adequately described in spite of the fact that the specification did not describe a large number of possible crystals. There was no mention of any need to describe an extensive number of crystals of the claimed polypeptide.

The arbitrary nature of the examiner's requirements are obvious when one considers the fact that polypeptides may exist in a multitude of states, for which the examiner has not required any support. For example, polypeptides can exist as amorphous precipitates, microcrystals, disordered crystals and semi-solids; yet, the examiner has selected solid, diffraction quality crystals as the embodiment for which an extensive amount of supporting disclosure is required. This is arbitrary and utterly unsupported by the case law. None of these embodiments require this extensive quantity of description for the types of claims at issue.

Claim rejections under 35 U.S.C. § 112(¶1)-Enablement

The examiner took the position that the specification has not taught how to make and use the crystals encompassed by the scope of the claims. The examiner is mistaken in view of several sources including those discussed below.

At the outset, the Examiner bears the initial burden of establishing that the claims are non-enabled. This burden has not been met. Citing *In re Wands*, the examiner alleged that the claims are non-compliant with the Enablement requirement. The *Wands* factors are addressed below:

Breadth of the claims[1]. The scope of the claims is not especially broad. The applicants are not claiming the universe. Rather, the applicants are merely claiming individual *species* of HDM2 polypeptides comprising *specifically defined* amino acid sequences. The claims are not directed, for example, to wide reaching genuses comprising all polypeptides within a defined percentage of amino acid sequence identity.

[1] These statements are not intended to disclaim any claim scope by way of estoppel or by any other means.

Furthermore, the scope of the present claims and the scope of claims covering only soluble polypeptides (as proposed by the examiner; see October 26, 2007 Office action at page 5, last paragraph) do not differ greatly. This point is apparent when one considers the nature of crystalline polypeptides. All compositions covered by the pending claims comprise the same primary structure (a specifically defined amino acid sequence). The amino acid sequence provides the bulk of the structural data available to describe the compositions covered by the claims. The major difference between one crystal embodiment of a given polypeptide and another is the three-dimensional arrangement of each polypeptide molecule in a lattice. Aside from this, crystals of a given polypeptide are, in large part, identical. Each crystalline polypeptide comprises the same specifically defined amino acid sequence. Thus, the fact that crystals are included within the claim scope does not render the claims, somehow, overly broad.

State of the prior art; Level of skill in the art; Level of predictability. The examiner argued that each of these elements points to an art that is highly unpredictable. The level of predictability in the art of molecular biology and crystallography does not weigh against the enablement of the claims

First, generating non-crystalline polypeptides described in the claims is not considered unpredictable; at least, the examiner has not alleged this. Moreover, any un-predictability of crystallography is mitigated by the amount of experimentation necessary. Briefly, the art of crystallography has become a high-throughput endeavor. Rapidly screening hundreds or thousands of crystallization conditions using commercially available kits is now possible. Moreover, screening can be

performed with a minimum of actual work on the part of a practitioner by use of robotics. Though the art has some level of unpredictability, advances in the field and, thus, the skill level of the ordinary practitioner, have limited the amount of work necessary to crystallize a given polypeptide. This point is discussed more below.

Direction provided. The amount of direction provided in the specification is adequate and the examiner is being overly stringent with regard to the amount of direction required.

First, the examiner does not appear to dispute that production of non-crystalline polypeptides is enabled. Example 1, in the specification, describes how to generate non-crystalline polypeptides. Moreover, such operations are routinely done in the molecular biology field.

Furthermore, Example 2 describes crystallization of an HDM2 F55Y/Y76H-tripeptide complex (starting at page 45, line 19); and Example 3 describes crystallization of an HDM2 Y76H-tripeptide complex (starting at page 63, line 1). In short, the applicants have selected two polypeptides and shown that they are crystallizable using relatively standard conditions and procedures. The methods and reagents used to crystallize the polypeptides were not especially exotic or unusual. Using the specification as a guide along with knowledge in the art, a practitioner would have been able to generate crystals of the HDM2 polypeptides covered by the claims. Indeed, using the many commercially available kits and robotic systems, a practitioner would conveniently have been able to generate a large variety of such crystals.

Quantity of experimentation necessary. Again, the quantity of experimentation necessary to make the non-crystalline polypeptides does not appear to be in dispute. Generation of

such compositions is conventional and routine in the art. The examiner has not established, however, that the amount of experimentation necessary to make the claimed crystals is undue. The examiner cited several articles and passages explaining that all protein crystallization is highly difficult and unpredictable (see *e.g.*, April 15, 2008 final office action starting at page 15). Specifically, statements from Branden *et al.*, Drenth *et al.*, Kierzek *et al.*, Wiencek *et al.*, Buts *et al.*, and Starzynski *et al.* were pointed out in support of this point. Essentially, examiner's argument is that crystallizing proteins would require undue amounts of experimentation and would be overly difficult for a crystallographer. We disagree with this point. Though making a crystal covered by the claims is not a simple task, the steps necessary for doing so are routine to a crystallographer.

Compliance with the Enablement requirement is not disproved by showing that *some* experimentation may be necessary. The amount of experimentation must be shown to be "undue" in order for non-compliance to be shown. Indeed, even large amounts of experimentation may be acceptable. The Federal Circuit explained in *In re Wands*:

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. *Ansul Co. v. Uniroyal, Inc.* [448 F.2d 872, 878-79; 169 USPQ 759, 762-63 (2d Cir. 1971), cert. denied, 404 U.S. 1018, 30 L. Ed. 2d 666, 92 S. Ct. 680 (1972)]. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed

858 F.2d 731, 737 (Fed. Cir. 1988) (emphasis added)

Moreover, the M.P.E.P. states:

> The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm"n 1983), aff'd. sub nom., *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985).

§2164.01 (emphasis added)

It is unclear how a crystallographer could view the amounts of experimentation necessary to crystallize an HDM2 polypeptide as undue or overly complex. It would seem apparent that crystallographers typically engage in crystallization of proteins such as HDM2. Such efforts often require screening of a large number of conditions. The theories behind protein crystallization have been known for decades as have the general types of screening steps necessary to identify crystallization conditions. For example, parameters such as salt concentration, precipitant concentration, polypeptide concentration, additive concentration, pH and temperature can be varied. So, an effort to identify crystallization conditions is very often a matter of varying such conditions. As the *Wands* court pointed out, the test is not merely quantitative. Whatever burden the experimentation would have must be evaluated *qualitatively*. This type of screening effort, though potentially involving a large scale screen, would be routine for a crystallographer who typically engages in such screening efforts and, thus, under *Wands*, is not undue.

In order to lessen the burden of large scale crystallization screens, automated screens have been developed. Such screens can

test thousands of crystallization conditions per day with very little physical effort on the part of any practitioner. For example, robotic workstations can automate liquid handling, plate sealing, incubation, image acquisition and analysis, and can also set up various incubation formats such as, *e.g.*, hanging drop, sitting drop and oil immersion. The existence of these screening options (which have been known in the art for years) further supports the argument that such screening is not undue.

Significantly, the examiner has not presented one shred of specific evidence to show that crystallization of the claimed HDM2 proteins would be especially complex for a crystallographer working in the field. The only evidence presented was generalized discussions in the literature regarding challenges in protein crystallization along with discussions in the literature relating to non-HDM2 crystals (*e.g.*, F17G fimbral adhesion).

The fact that generation of crystals of the claimed polypeptides would not require undue amounts of experimentation does *not*, in any way, indicate that the claimed compositions are obvious under 35 U.S.C. § 103(a). Clearly, there is no teaching or suggestion of the claimed compositions in the prior art. A practitioner would have had no reason, prior to the instant invention, to modify known HDM2 polypeptides in a manner which arrives at the claimed polypeptides.

The Federal Circuit addressed what is required to enable a DNA-based invention stating that "[f]or DNA sequences, that means disclosing how to make and use enough sequences to justify grant of the claims sought." *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991) (citing *In re Angstadt*, 537 F.2d 498, 502 (CCPA 1976)) (citations omitted). Notably, the court did not state that crystalline DNA molecules must be characterized in order for the enablement requirement to be met.

As discussed above, this statement would apply to polypeptides given the similarities between the molecules. The present claims disclose the amino acid sequences of the claimed polypeptides and, thus, at least under *Amgen*, are enabled.

The Comments of the USPTO on Trilateral Project WM4, "Comparative study on protein 3-dimensional (3-D) structure related claims" are in accord with this holding. The Comments considered the enablement of the hypothetical claim:

> An isolated and purified molecule comprising a binding pocket of protein P defined by the structural coordinates of amino acid residues 223, 224, 227, 295, 343, 366, 370, 378 and 384 according to Figure 1.

The specification explicitly discussed X-ray diffraction data of the claimed protein. There was no mention whatsoever, in the discussion of enablement, of limiting the claims to non-crystalline proteins. The claim was deemed enabled. The discussion stated that "[w]ith respect to the enablement requirement, the specification enables the full-length protein P and the specifically disclosed fragments."

The "Training Materials for Examining Patent Applications with Respect to 35 USC Section 112, First Paragraph-Enablement of Chemical/Biotechnical Applications", discussed a hypothetical claim at Example 5E (abbreviated):

> 1. A peptide consisting of the sequence. . .

; wherein the application disclosed the sequence and how to make such polypeptides. Respecting the "how to make" prong of enablement, the claim was found sufficiently enabled according to the materials.

As further confirmation of the USPTO policy with regard to claims comprising the general format of the instant claims, the

applicants point out that Supervisory Patent Examiner Michael Woodward gave a presentation at the Biotechnology/Chemical/Pharmaceutical Customer Partnership of January 14, 2003 (available on the Ed Cabic webpage at http://www.cabic.com/ejc/BCPCP011403/MWoodward_3D.ppt). In this presentation, Examiner Woodward presented a hypothetical claim:

> Claim 2. An isolated and purified polypeptide consisting of a portion of protein P starting at one of amino acids 214 to 218 and ending at one of amino acids 394 to 401 of protein P as set forth in SEQ ID NO: 1.

In the specification, the applicants presented SEQ ID NO: 1 and 3-dimensional structural data for the protein. Specifically, Examiner Woodward said:

> The description teaches that all possible peptides that begin with any amino acid from position 214 to 218 and end with any amino acid from position 394 to 401 of SEQ ID NO: 1 are protein domains that fold into an active binding pocket of protein P. This ability was confirmed by X-ray diffraction data.

Regarding compliance with the Enablement requirement, Examiner Woodward stated:

> Claim 2 complies with both the enablement and written description requirements of 35 U.S.C. §112, ¶1.

This hypothetical was taken from the Trilateral Comparative Study on Protein 3-dimensional (3-D) structure related claims (also discussed above).

Finally, USPTO examination policy, apparently, has been such that claims of this type are to be considered enabled if the primary structure (*i.e.*, amino acid sequence) of the claimed

polypeptide is disclosed. This policy is evident both in the Trilateral Agreement discussions set forth above as well as the Office's extensive history of allowing such claims on this basis. Though the examination of one application is not *stare decisis* respecting the examination of another; the applicants are entitled to a uniform and fair standard of examination. Moreover, patents granted under this policy are presumed valid. 35 U.S.C. § 282. The implication of the rule applied to the appealed claims is that the thousands of similar claims granted to this point are invalid. It would strain credulity to state that the instant claims are, somehow, uniquely non-enabled in spite of the apparent enablement of the multitude of similar polypeptide claims which have been granted heretofore. It should be noted that the examiner initially applied the established examination standard, in this case, before switching to this new standard during examination. Specifically, in the August 26, 2005 office action, the examiner stated that the specification was enabling for the polypeptides of SEQ ID NO: 6, 8, 10 and 12 (see page 12, 2nd full sentence). Likewise, the apparent USPTO examination policy has also been that claims of this type are sufficiently described on the basis of disclosure of the polypeptide amino acid sequence. This has been a long-standing policy which is being ignored in this case.

A counter-argument offered by the examiner is that the claims at issue in the cases cited and in the Guideline and Comments presented did not include crystals and, thus, are not applicable to the instant rejections for lack of written description and enablement. The examiner stated that:

> There is no evidence of record or line of reasoning that the claims of the cited case law were intended as encompassing crystalline forms of

> the polypeptide. (Final Office Action mailed Apr. 15, 2008, p. 10)

We disagree and Federal Circuit case law disagrees with this mode of claim interpretation. For example, in *Liebel-Flarsheim Co. v. Medrad, Inc*, the Federal Circuit stated that "absent a clear disclaimer of particular subject matter, the fact that the inventor may have anticipated that the invention would be used in a particular way does not mean that the scope of the invention is limited to that context." 358 F.3d 898 (Fed. Cir. 2004) (quoting *Northrop Grumman Corp. v. Intel Corp.*, 325 F.3d 1346, 1355 (Fed. Cir. 2003) (citing *Brookhill-Wilk, LLC v. Intuitive Surgical*, Inc., 334 F.3d 1294, 1301 (Fed. Cir. 2003); and *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1328 (Fed. Cir. 2002)). In the absence of a disclaimer, the claims are not limited to what is discussed in the specification. In *In re Bigio*, the Federal Circuit stated:

> this court counsels the PTO to avoid the temptation to limit broad claim terms solely on the basis of specification passages. *In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989). Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification or prosecution history when those sources expressly disclaim the broader definition.

381 F.3d 1320, 1324 (Fed. Cir. 2004) (referring to *Liebel-Flarsheim*, 358 F.3d at 906-909).

The examiner's counter-argument that the cited case law does not mention crystals weighs in favor of our argument. Given the presumption that claims will include subject matter not specifically disclaimed, this would suggest that the claims in the cases cited would include crystals. Certainly, none of the

cited cases state that crystals were excluded from the claim scope.

There is no evidence such a disclaimer was made in any of the cases discussed and, indeed, it is highly unlikely. Given the presumption against reading such limitations into claims, it would be inappropriate to do so when determining the scope of the holdings, Guidelines and Comments discussed herein. Thus, the claims discussed above would have been interpreted as encompassing *any* polypeptide exhibiting the elements specified-crystalline or non-crystalline.

The examiner, citing *Ex parte Kubin*, also argued that the Guidelines and Comments cited in the arguments in support of patentability were not persuasive since such sources do not create a rigid test. 2007-0819 (B.P.A.I., 2007). While the applicants are not disputing this point, the Board, in *Kubin*, did not approve disregarding these sources entirely. The examiner, however, seems to summarily reject the Guidelines and Comments for no apparent reason. At the very least, when the facts warrant such disregard for the Guidelines and Comments, some explanation as to why they are not applicable would appear appropriate. The examiner discussed the reasons he believed the claims to be non-compliant with §112, however, no explanation as to why the Guidelines and Comments were disregarded was ever made. This disregard for the Guidelines is at odds with that of the Federal Circuit. Though the Guidelines are not binding precedent on the courts, the Federal Circuit has repeatedly recognized their persuasive value and has resorted to the Guidelines for guidance on the Written Description requirement. See *e.g.*, *Univ. of Rochester*, 358 F.3d at 925; *Invitrogen*, 429 F.3d at 1072; and *Enzo Biochem.*, 323 F.3d at 964. In the absence

of any specific reason for disregarding such Guidelines and Comments, ignoring them appears arbitrary and improper.

The appellants submit that the rejected claims are sufficiently described and enabled and that the claim rejections are not well founded. The appellants request reversal of all rejections.

Respectfully submitted,

Date: 2/25/2009

Thomas Triolo, Ph.D., J.D.
Registration No. 48,001
Attorney for Applicants/Appellants

Schering-Plough Corporation
Patent Department; K-6-1, 1990
2000 Galloping Hill Road
Kenilworth, NJ 07033
908-298-2347

APPENDIX: CLAIMS ON APPEAL

2. A purified polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 and SEQ ID NO: 12.

36. The polypeptide of claim 2 comprising the amino acid sequence set forth in SEQ ID NO: 6.

37. The polypeptide of claim 2 comprising the amino acid sequence set forth in SEQ ID NO: 8.

38. The polypeptide of claim 2 comprising the amino acid sequence set forth in SEQ ID NO: 10.

39. The polypeptide of claim 2 comprising the amino acid sequence set forth in SEQ ID NO: 12.